

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently amended) A method of preparing DNA fragments from a sample of nucleic acids to be analyzed, which method ~~[[is characterized in that it]]~~ comprises ~~[[the selective fragmentation of said]]~~ selectively fragmenting the nucleic acids by means of at least the following steps:

I. for a first selection of short fragments~~[[, comprising]]~~:

a) ~~[[the preparation of]]~~ preparing first double-stranded DNA fragments F1 using at least one restriction enzyme E1 capable of randomly fragmenting the sample of nucleic acids to be analyzed, generating said DNA fragments F1 with blunt or cohesive ends,

b) ~~[[the ligation of]]~~ ligating the ends of said DNA fragments F1 obtained in step a) to at least one adapter AA', so as to form a unit - located at the junction of the complementary end of said adapter and of the 5' end of said fragments F1, such that:

~~[[ - ]]~~the sequence of said unit is that of the first N-x base pairs of the recognition site - comprising N base pairs - of a restriction enzyme E2, the cleavage site of which is located

downstream of said recognition site, with  $1 \leq x \leq N-1$ , and  
[[[-]]its 3' end - located 5' of said DNA fragments F1 - is that  
of the restriction site of the E1 restriction enzyme, so as to  
obtain DNA fragments F'1,

- c) [[the cleavage of]] cleaving the DNA fragments F'1 obtained in
  - b) [[-]] in the vicinity of their 5' end [[-]] using said restriction enzyme E2, so as to select a fraction of short fragments F2,
  - d) [[the purification, by any appropriate means, of]] purifying said fraction of short fragments F2,  
and, optionally,

II. for a second selection of one or more subset(s) of fragments from the fraction of short fragments F2 obtained in step d) [[-  
~~in accordance with the following steps~~]]:

- e) [[the ligation of]] ligating the free end (not linked to the adapter AA') of short fragments F2 obtained in d) to at least a second complementary adapter BB' (production of fragments F'2), and
- f) [[the amplification of]] amplifying the short fragments F'2 linked to said adapters (AA' and BB'), using at least one pair of appropriate primers, at least one being optionally labeled at its 5' end, so as to select at least one subset of short fragments F'2 from the fraction of short fragments F'2

obtained in d).

2. (Currently amended) The method as claimed in claim 1, [[characterized in that]]wherein step a) is carried out with two different E1 restriction enzymes, E1<sub>A</sub> and E1<sub>C</sub>, such that:

[[ - ]]at least one generates cohesive ends, different from those optionally generated by the other restriction enzyme, and

[[ - ]]the 3' end of the E1<sub>A</sub> restriction site is that of the unit as defined in step b).

3. (Currently amended) The method as claimed in claim 2, [[characterized in that]]wherein one of the enzymes cleaves frequently and the other rarely.

4. (Currently amended) The method as claimed in claim 3, [[characterized in that]]wherein:

[[ - ]]the enzyme that cleaves frequently is the enzyme E1<sub>A</sub>, which enzyme E1<sub>A</sub> generates at least one end of a fragment F1 that binds to the adapter AA' in step b), and

[[ - ]]the enzyme E1<sub>C</sub> that cleaves rarely, generates at least one end of a fragment F1, which binds, in step b), to a second adapter CC' that is different from the adapter AA'.

5. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 4]]~~claim 1, ~~[[characterized in that]]~~wherein steps a) and b) are carried out simultaneously.

6. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 5]]~~claim 1, ~~[[characterized in that it]]~~which further comprises ~~[[an additional step consisting of the purification of]]~~purifying the fragments less than 1000 bp, prior to the ligation step b).

7. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 6]]~~claim 1, ~~[[characterized in that]]~~wherein the adapter AA' as defined in step b) comprises, at the 3' end of the strand A ~~[[and/or]]~~or 5' end of the strand A', or both, a zone 1 of approximately 1 to 8 bases or base pairs, which is partially or completely identical or complementary to the restriction site of the enzyme E1, which zone 1 is chosen so as to reconstitute the sequence of the first N-x bases or base pairs of the recognition site of the restriction enzyme E2, by ligation of said adapter AA' to the ends of said DNA fragments obtained in a).

8. (Currently amended) The method as claimed in claim 7, [[characterized in that said]]wherein zone 1 includes one or more mismatches with the sequence of said cleavage site of the restriction enzyme E1.

9. (Currently amended) The method as claimed in [[any one of claims 1 to 8]]claim 1, [[characterized in that]]wherein the adapter as defined in step b) comprises, upstream of the zone 1, a zone 2 of at least 6 base pairs.

10. (Currently amended) The method as claimed in [[any one of claims 1 to 9]]claim 1, [[characterized in that]]wherein the adapter as defined in step b) comprises at least one base located between the zone 1 and the zone 2, different from that which, in the cleavage site of the restriction enzyme E1, is immediately adjacent to the complementary sequence corresponding to the zone 1.

11. (Currently amended) The method as claimed in [[any one of claims 1 to 10]]claim 1, [[characterized in that]]wherein the adapter as defined in step b) comprises a phosphate residue covalently linked to the 5' end of the strand A'.

12. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 11]]~~claim 1, ~~[[characterized in that]]~~wherein, when said method consists of a single selection of short fragments according to steps a) to d), it comprises at least one additional step b'), c') ~~[[and/or]]~~or d') or a combination thereof~~[[consisting of the amplification of]]~~ comprising amplifying the fragments F'1 or F2 using an appropriate pair of primers, preferably a pair of labeled primers.

13. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 12]]~~claim 1, ~~[[characterized in that]]~~wherein the adapter AA' as defined in step b) is linked, at the 5' end of its strand A, to an appropriate label, in particular a label for detecting nucleic acid hybrids or a label that ~~[[can attach]]~~is attachable to a functionalized solid support.

14. (Currently amended) The method as claimed in ~~[[any one of claims 2 to 13]]~~claim 1, ~~[[characterized in that]]~~wherein the 5' end of the strand C' of the adapter CC' is linked to a label, which label ~~[[can attach]]~~is attachable to a functionalized solid support.

15. (Currently amended) The method as claimed in ~~[[any one of claims 12 to 14]]~~claim 1, ~~[[characterized in that]]~~wherein the fragments F'1 obtained in step b) or b') are brought into

contact with said functionalized support prior to the cleavage step c), and the fraction of short fragments F2 of step d) corresponds to the fraction of fragments that is either retained on said support (adapter AA' linked to the label that attaches to the support) or free (adapter CC' linked to the label that attaches to the support).

16. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 11 and 13 to 15]]~~claim 13, ~~[[characterized in that it]]~~which comprises, in step e), ~~[[the ligation of]]~~ligating several different complementary adapters (B<sub>1</sub>B<sub>1</sub>', B<sub>2</sub>B<sub>2</sub>', etc.), each comprising, at the 5' end of the strand B or at the 3' end of the strand B', a specific sequence of 1 to 10 bases.

17. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 11 and 13 to 16]]~~claim 13, ~~[[characterized in that]]~~wherein said adapter BB' as defined in step e) comprises a phosphate residue covalently linked to the 5' end of the strand B.

18. (Currently amended) The method as claimed in ~~[[any one of claims 1 to 11 and 13 to 17]]~~claim 13, ~~[[characterized in that]]~~wherein one of the primers as defined in step f) is linked, at its 5' end, to an appropriate label.

19. (Currently amended) The method as claimed in ~~any one of claims 1 to 18~~ claim 1, ~~characterized in that it~~ which comprises an additional step d") or g) ~~consisting of the~~ comprising obtaining~~[, by any appropriate means, of]~~ single-stranded fragments from the short fragments F2 obtained in step d) or d') or else from the short fragments F'2 obtained in step f).

20. (Currently amended) The method as claimed in ~~any one of claims 1 to 19~~ claim 1, ~~characterized in that it~~ which further comprises ~~[an additional step consisting of the purification]~~ purifying~~[, by any appropriate means, of]~~ the amplification products obtained in step b'), c'), d') or f) or of the single-stranded fragments obtained in step d") or g).

21. (Currently amended) A short DNA fragment, representing a genetic marker, ~~that can be~~ obtained by ~~means of~~ the method as claimed in ~~any one of claims 1 to 20, characterized in that it~~ claim 1, which has a sequence of less than 100 bases or base pairs, comprising at least one specific sequence consisting of a fragment of genomic sequence or of cDNA sequence bordered, respectively, by the recognition site and the cleavage site of a restriction enzyme E2, the cleavage site of which is located downstream of said recognition site, such that the 5'

end of said specific sequence corresponds to the last x base pairs of the recognition site - having N base pairs - of said enzyme E2, with  $1 \leq x \leq N-1$ , said marker including, at each end, at least 6 bases or 6 base pairs of nonspecific sequence.

22. (Currently amended) The DNA fragment as claimed in claim 21, [[characterized in that it]]which is a single-stranded fragment.

23. (Currently amended) The DNA fragment as claimed in claim 21~~[[or claim 22, characterized in that it]]~~[[which is linked, at one of its 5' ends, to an appropriate label.]]

24. (Currently amended) A DNA chip, characterized in that it comprises a DNA fragment as claimed in ~~[[any one of claims 21 to 23]]~~[[claim 21.]]

25. (Cancelled).

26. (Cancelled).

27. (Currently amended) A method of hybridizing nucleic acids, [[characterized in that it uses]]which comprises hybridizing the nucleic acids with a DNA fragment as claimed in ~~[[any one of claims 21 to 23 or a DNA chip as claimed in claim 24]]~~[[claim 21.]]

28. (Currently amended) A kit for carrying out ~~[[a method of hybridization, characterized in that it comprises at least one DNA fragment as claimed in any one of claims 21 to 23 or a DNA chip as claimed in claim 24]]~~the method of claim 27.

29. (Cancelled).

30. (Cancelled).

31. (Currently amended) A kit for carrying out the method as claimed in ~~[[any one of claims 1 to 20]]~~claim 1, ~~[[characterized in that it]]~~which comprises at least one adapter AA' as defined in ~~[[any one of claims 7 to 11, and a restriction enzyme E2 as defined in claim 1]]~~claim 7, and a restriction enzyme E2 as defined in claim 1.

32. (Currently amended) The kit as claimed in claim 31, ~~[[characterized in that it also]]~~which further comprises at least one adapter BB' as defined in claim 1~~[[, 16 or 17]]~~, and a pair of primers as defined in claim 1 ~~[[or 18]]~~.

33. (New) The kit is claimed in claim 28, which comprises at least one DNA fragment as claimed in claim 21.

34. (New) The kit as claimed in claim 28, which comprises at least one DNA chip as claimed in claim 24.

35. (New) The kit as claimed in claim 33, which further comprises an oligonucleotide probe complimentary to the DNA fragment.

36. (New) A method of hybridizing nucleic acids, which comprises hybridizing the nucleic acids with a DNA chip as claimed in claim 24.